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THE COUNCIL FOR TOBACCO RESEARCH–U.S.A., INC.

110 EAST 59TH STREET
NEW YORK, N. Y. 10022
(212) 421-8985

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JUL 1 1975

Application for Research Grant
(Use extra pages as needed)

Date: July 1, 1975

1. Principal Investigator (give title and degrees): Walter B. Essman, Ph.D., M.D.
Professor of Psychology & Biochemistry

2. Institution & address: Queens College of the City University of New York
65-30 Kissena Boulevard
Flushing, New York 11367
and
The Research Foundation of the City University of New York
1411 Broadway, New York, New York 10018

3. Department(s) where research will be done or collaboration provided:

Department of Psychology, Queens College of the City University of New York

4. Short title of study: "Metabolic Response to Stress--Tobacco Smoke Interactions"

5. Proposed starting date: January 1, 1976

6. Estimated time to complete: 3 years.

7. Brief description of specific research aims: Several methods developed in our laboratory have enabled us to utilize cellular models in which specific biologically active molecules can be tested. Such molecules include both transmitter (norepinephrine, 5-Hydroxytryptamine, acetylcholine), or trophic (5-hydroxytryptamine, dopamine) agents, unique to such tissue. Specifically, developmental (age-dependent) and pathological (tissue changes) concommittant with acute and chronic stress stimuli have been studied. Their interaction with tobacco smoke and/or nicotine have been further considered. It is the purpose of this investigation to study tobacco smoke (including its gas phase) and biologically active constituents (nicotine) insofar as they interact with stress-induced stimuli in rodents.

Experimental description of the metabolic and molecular events associated with stress and its adaptation are investigated in several functional systems (brain, heart, lung, and gastro-intestinal tract).

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7. Brief description of specific research aims: (Continued)

The biologically active molecules altered by acute or chronic stress will be studied in the above mentioned tissue systems. Alterations in content, metabolism, uptake and synthesis will be studied with in vivo and in vitro methods in order to assess: 1) effects of acute or chronic cigarette smoke exposure and 2) acute and chronic effects of nicotine. The overall aim of this project is to provide a general description of those factors implicit in stress which cause molecular changes and how such effects are modified by interaction with nicotine.

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8. Brief statement of working hypothesis:

Previous research has shown that models of acute and chronic stress may be found in basic cellular mechanisms. The effects of tobacco smoke and/or nicotine can be measured in such model systems. On this basis, several working hypotheses have been formulated. The interaction of the effects of stress and nicotine alter the cellular and/or molecular effects produced by stress. The cellular mechanisms altered by stress will, upon appropriate presentation, show adaptation. On the basis of this general overall hypothesis, several specific working hypotheses have been developed: a) cellular changes in the central nervous system (storage, synthesis, and uptake of neurotransmitters by neurons, glia, and synaptosomes) are highly sensitive to and will occur with stress and nicotine; (b) pulmonary epithelial cells and pulmonary alveolar macrophages are sensitive to the effects of tobacco smoke. Differences in amine concentration in this tissue (epithelial cells) or amine interaction with tissue products (macrophages) will occur as a function of 1) age; 2) strain; 3) sex; and 4) the frequency and duration of tobacco smoke exposure; c) cardiac catecholamine uptake and release is altered by acute and chronic stress. Such alteration is dependent upon genetic differences and may be altered by cigarette smoke and/or nicotine. Experimentally induced diabetes mellitus or the use of catecholamine receptor antagonists will induce pathological changes in cardiac tissue. These changes will alter the effect of cigarette smoke upon amine metabolism of this tissue and will also change the pharmacological effect and tissue distribution of cardiolytic drugs; specifically, digoxin; (d) gastrointestinal tissue and its 5-HT containing storage depots will show morphological as well as biochemical changes in the development of stress-induced gastric ulcers. Such stress-induced changes and their recovery are sensitive to the effects of cigarette smoke. The stress-induced pathological changes may be predicted by changes in 5-HT; this relationship will serve as a basis for other predictions of effect from cigarette smoke and/or nicotine.

The working hypotheses underlying this proposal, therefore, concern themselves with tobacco smoke (nicotine) - stress-induced interactions as they apply to four tissue levels, the cellular and organelle specificity of which will reflect differences in response to systemic stress and physiological levels of nicotine.

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9. Details of experimental design and procedures

A large number of stressor agents and/or events have been utilized to produce physiological changes (Selye, 1950). There are several stressor conditions which have been reliably used in rodents (rats, mice, and guinea pigs); for acute stress, both restraint and electroshock will be utilized. Both of these stressor conditions can be varied as to (a) duration, (b) frequency, (c) time of day at which they are initiated and (d) age of the animal as well as its strain.

Chronic stress will be provided through isolation housing; this stress and its sequalae has been extensively documented in experiments carried out in this laboratory for more than 10 years. Isolation stress can be titrated in terms of duration and can be carried out for animals of different ages as well as strain.

The proposed experiments will deal with peripheral (pulmonary, cardiac, and gastrointestinal) as well as central nervous system cellular and subcellular changes which accompany or follow either acute or chronic stress; the extent to which these effects interact with tobacco smoke and/or nicotine will be described.

In peripheral tissues, the lung, heart and gastrointestinal tissue will be studied, specifically with regard to their relevant transmitter or trophic agents; i.e., 5-hydroxytryptamine, norepinephrine, or dopamine. The areas of the brain will be divided into functionally distinct regions; i.e., limbic region, basal ganglia, etc.

The proposed experiments will utilize both in vivo as well as in vitro techniques. The parameters to be specifically investigated include (1) the duration of stress; (2) the frequency with which stress stimulation is presented; (3) diurnal variations in the presentation of stress stimulation; (4) age differences in the effect of stress and (5) strain differences in the effects of stress. Exposure to tobacco smoke by means of a standardized nicotine content cigarette will be provided to an animal in a Walton Upright Cigarette Smoking machine; control animals will be exposed to filtered cigarette smoke (filtration

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of nicotine and exposure to gas phase only), or an equivalent volume and duration of room air provided to the smoking chamber. The parameters of the smoke exposure to be considered will include (a) frequency of smoke exposure, (b) duration of smoke exposure, and (c) time of day at which smoke exposure is provided.

Other parallel in vivo and in vitro studies will be carried out utilizing nicotine and several of its biologically active metabolites; these will be administered either in vivo along with the stress conditions, or will be utilized in vitro in those studies where tissue from stressed animals will be utilized. Nicotine will be given either as the alkaloid or in the bitartrate form. Nicotine metabolites will include those which in previous experiments have been clearly demonstrated to possess biological activity (Essman, 1973 (5)); (capable of being taken up by the cerebral cortex and basal ganglia). These compounds are cotinine, 3-pyridylacetic acid, and the analog, nornicotine. In vivo doses of these derivatives have been established in previous studies, and the in vitro concentration to be utilized will all be at 10^{-6}M, or less.

The following series of experiments will be specifically carried out for the tissue systems outlined.

I. Effects of Stress-Nicotine Interactions Upon Brain Tissue:

Studies with brain tissue will include a regional comparison of three major functional constituents -- neuronal cell bodies, glia, and synaptosomes. The regions of the brain to be considered will include (a) cerebral cortex, (b) diencephalon, (c) basal ganglia, (d) limbic region and (e) cerebellum. For each of these regions, standardized fractionation methods (differential and sucrose or sucrose-ficoll density gradient centrifugation) will be applied

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(Essman, 1973 (3)) or combined with newly developed methods; the latter techniques (i.e., isolation of neuronal perikarya from adjacent glia have been developed in our laboratory. These methods for cell separation yield highly enriched fractions of either neurons, glia or synaptosomes (synaptic nerve endings). The purity and morphology of each such fraction can be confirmed by the use of enzyme markers (acetylcholinesterase-neurons; butyrylcholineserase-glia) and/or scanning electron microscopy. The purity of these fractions will be verified with such markers and ulstrastructural correlates.

Thus, for brain tissue, it will be possible to assess the region in which the effects of stress and/or tobacco smoke are manifest, the cellular specificity of this effects, and the synaptic change produced. The basic experiments that will concern the regional, cellular and subcellular effects of stress-tobacco smoke interactions will involve:

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A) Specific Uptake of Biogenic Amines: This procedure will be carried out in vitro with the cell fractions (either neurons, glia, or synaptosomes) incubated in 1.25 µc per ml. of either C^{14}-labelled 5-hydroxytryptamine, norepinephrine, or dopamine for 45 minutes at 37°C in a standardized Krebs-Henselite medium ventillated with 95% O_2 and 5% CO_2. Measurement of the uptake of these biogenic amines will be made for the in vivo conditions of stress-tobacco smoke and/or nicotine interactions mentioned above. A further series of experiments will test nicotine or active metabolites thereof in vitro to assess effects upon amine uptake. Substantial data already obtained have indicated that concentrations of nicotine as little as 2.5×10^{-7} will exert highly significant effects on uptake. For example, 5-HT and norepinephrine uptake were reduced by nicotine in neurons and glia of the cerebral cortex. Diencephalic neurons had significantly increased catecholamine uptake stimulated by nicotine, but glia from that region

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showed significantly reduced catecholamine uptake.

Decreased cellular uptake of amines is usually an indication of enhanced excitability and is one of the mechanisms by which antidepressant drugs exert their effect. In this context, the excitatory effect of nicotine, in vitro, is consistent with the electrophysiological localization in vivo. The major differences between these similar effects, however, is that the concentrations required for electrophysiological changes are 100 to 1000 times greater. Therefore, the proposed methodology, aside from utilizing physiological concentrations of nicotine has also been shown sensitive to these low levels.

B) Cerebral Protein Synthesis: The in vitro incorporation of C^{14}-labelled leucine into proteins isolated from either neurons, glia, or synaptosomes isolated from several regions of the rodent brain has been reported (Essman, 1973 (6); 1974 (11)). After incubation (45 minutes under physiological conditions), proteins will be precipitated and assessed for incorporation of the labelled amino acid. These studies will evaluate stress-tobacco smoke interactions and assess the in vitro effects of nicotine and its metabolites. In the latter regard, nicotine concentrations as little as 2.5×10^{-7}M have been shown to alter amino acid incorporation into specific neuronal as well as glial proteins; for example, of several brain regions sampled, only the cells of the basal ganglia showed statistically significant increases in protein synthesis from nicotine (59% for neurons, 24% for glia). The increase in protein synthesis at the cellular level usually suggests excitation. The specificity of this effect from physiological concentrations of nicotine (basal ganglia) indicates the selectivity of the method for assessing the effects of nicotine at low levels.

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II. Effects of Stress-Nicotine Interactions Upon Pulmonary Tissue and Products:

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These experiments will consist of two basic protocols; the first will concern the effects of stress-tobacco smoke interactions upon the concentration and release of 5-hydroxytryptamine in pulmonary epithelial tissue; the second will concern in vivo stress and/or smoke effects upon the in vitro interaction of pulmonary alveolar macrophages with 5-hydroxytryptamine. These effects will be defined for age, sex, strain, and diurnal variations; all of these variables appear to contribute significantly to the effects of tobacco smoke and/or nicotine upon stress (Essman, 1974 (9, 10), 1975 (15). The tissue preparation, extraction and assay of 5-hydroxytryptamine has been previously described in numerous publications as well as progress reports from this laboratory; this involves standardized procedures for the spectrofluorometric determination of this biogenic amine (see Essman, recent publications).

The harvesting of pulmonary alveolar macrophages by bronchopulmonary lavage utilizes sterile Tullis solution maintained at a pH of 7.4; use of subsequent magnesium-free glucose medium precludes cellular replication. The number of macrophages utilized in the binding studies and their morphological characteristics will be assessed by scanning electron microscopy of fixed (gluteraldehyde) preparations. Binding studies with this preparation will utilize C^{14} labelled 5-hydroxytryptamine (0.1μc) in an equilibrium dialysis chamber through a 0.62 membrane for 16.5 hours. 5-HT binding per macrophage can be precisely calculated and related to the in vivo conditions (nicotine, gas phase, etc.) which produce qualitative changes in the macrophage. Such changes, already documented in preliminary studies include strain-related changes in the number of macrophage binding sites (increased in DBA mice, decreased in C3H mice) and macrophage elongation with increased furrowing. The in vitro effects of physiological concentrations of nicotine (10^{-7}M) and its metabolites upon 5-hydroxytryptamine binding by macrophage will be assessed by the addition of these compounds to the chamber

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before equilibrium dialysis is begun. Such factors as competition for the macrophage binding sites with nicotine will be determined using radiolabeled nicotine. No such studies have appeared in the experimental literature; their significance lies in the quantitative assessment of macrophage response (binding and morphology) following smoke exposure and induction of increased 5-HT by smoke. From preliminary data, it appears that increased or decreased macrophage binding sites for 5-HT only occur in those strains where pulmonary 5-HT is elevated by smoke. We believe that this relationship, clarified through the proposed experiments, will provide a novel definition of macrophage viability.

III. Effects of Stress-Nicotine Interactions Upon Cardiac Tissue:

Two general experimental procedures will be carried out with cardiac tissue. These will consist of both in vivo and in vitro experiments which relate stress and the effects of tobacco smoke, described above, to cardiac catecholamine uptake and to digoxin distribution. Previous studies have provided convincing evidence to show that cardiac norepinephrine (NE) uptake is severely reduced by stress (immobilization of mice for 8 minutes reduced cardiac NE uptake by 66%); reduced NE uptake may be reversed as adaptation to such stress (as measured by a successive decrease to normal of plasma corticosterone level) occurs; (e.g., after 21 days of successive episodes of immobilization, cardiac NE uptake had returned to within baseline limits). Animals, while immobilized, were exposed to 8 minutes of cigarette smoke for one week and showed only a 20% reduction in cardiac NE uptake. This finding suggests that cigarette smoke may exert a protective effect against stress-induced cardiac NE uptake reduction. The experiments will investigate (1) the in vivo uptake of norepinephrine (NE) and dopamine (DA) by cardiac tissue; (2) the in vitro uptake of these catecholamines by whole tissue and (3) uptake and distribution in subcellular fractions (nuclei, mitochondria, microsomes)

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thereof. Stress, acute (electroshock) as well as chronic (isolation), can markedly increase the cardiac distribution of digoxin (acute stress = 51%; chronic = 103%), an important cardiac glycoside (Essman, 1973 (8)). Both in vivo as well as in vitro studies will be conducted to assess changes in cardiac digoxin distribution resulting from stress-tobacco smoke interactions.

The significance of these studies lies in the potential functional impairment of cardiac activity by stress and its reversal by tobacco smoke Furthermore, digoxin toxicity appears to be potentiated by stress; tobacco smoke and/or nicotine may modify this effect.

Further studies will be carried out utilizing a model of experimental diabetes mellitus (EDM), induced in the rat by means of alloxan treatment (65 mg/kg i.v.). Such an experimental model has been tested by preliminary studies in this laboratory; fasting blood glucose levels are elevated by 2 weeks post-treatment, to approximately 280 mg%. The object of this animal model is to provide baseline data for a systemic stress condition wherein both cardiac catecholamine uptake and digoxin distribution may be assessed. Diabetic rats and normoglycemic controls will be exposed to tobacco smoke or treated with nicotine. The cardiac tissue will be fractionated into its subcellular constituents. In vitro studies will involve the effects of physiological levels of nicotine (10^{-7} - 10^{-5}M) and its active metabolites. Catecholamine uptake and digoxin distribution in the cardiac tissue and its organelles will be documented.

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Preliminary data from our laboratory have been obtained using normoglycemic (mean blood glucose = 105 mg%) and alloxan-induced hyperglycemic (mean blood glucose = 315 mg%) rats. Digoxin uptake was measured in vitro; the rate of uptake was significantly lower among the diabetic rats, and nicotine (10^{-5}M) lowered digoxin

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uptake of the cardiac tissue even more (Table 1).

Table 1

Uptake of H^3-Digoxin (cpm/mg protein)
by Cardiac Tissue from Normal and Diabetic Rats
as a Function of In Vitro Nicotine (10^{-5}M)

IN VIVO CONDITION	IN VITRO TREATMENT	
	0.9% NaCl	Nicotine
NORMOGLYCEMIC	124.4	114.2
HYPERGLYCEMIC	102.2*	91.8*

*p<.02

Norepinephrine uptake by cardiac tissue from diabetic rats was significantly reduced; nicotine (10^{-5}M) reduced cardiac norepinephrine uptake in normoglycemic rats, but did not alter the already reduced rate ofuptake in diabetic rats (Table 2).

Table 2

Uptake of C^{14}-Norepinephrine
(cpm/mg Protein) by Cardiac Tissue from Normal and
Diabetic Rats as a Function of In Vitro Nicotine (10^{-5}M)

IN VIVO CONDITION	IN VITRO TREATMENT	
	0.9% NaCl	Nicotine
NORMOGLYCEMIC	4988.2	1406.2*
HYPERGLYCEMIC	1286.5	1330.6

p<.01

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Cardiac mitochondrial protein synthesis was lowered in diabetic rats; nicotine lowered cardiac mitochondrial protein synthesis in normoglycemic rats, but in diabetic rats it led to increased synthesis (Table 3).

Table 3

Incorporation of C^{14}-Leucine Into
Proteins from Several Subcellular Fractions of
Rat Cardiac Tissue from Normal or Diabetic Animals: Effects of Nicotine

IN VIVO CONDITION	SUBCELLULAR FRACTION	IN VITRO TREATMENT	
		0.9% NaCl	Nicotine
NORMAL	NUCLEI	86.9	87.2
	MITOCHONDRIA	261.9	162.5*
	MICROSOMES	63.1	56.1
DIABETIC	NUCLEI	83.7	96.9
	MITOCHONDRIA	154.5	196.6*
	MICROSOMES	69.3	76.9

$p<.02$

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IV. Effects of Stress-Nicotine Interactions Upon Gastrointestinal Tissue:

The pathological change in gastrointestinal tissue with which the proposed experiments are concerned is the development of gastric ulcers in stressed animals. There have been no clear indications as to the significance of tobacco smoke upon ulcerogenesis. Several of our previous studies have indicated an etiological relationship between stress-induced gastric ulceration and gastrointestinal 5-hydroxytryptamine content and metabolism (Essman, et al., 1971); e.g. immobilization stress facilitated gastric ulcerogenesis in the pyloric region;

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stress-ulcerated mice had elevated gastric tissue pH and increased gastric 5-HT content.

This series of studies will measure 5-hydroxytryptamine content (utilizing standardized spectrofluorometric methodology) and turnover (utilizing steady-state kinetics methods) to evaluate the in vivo contributions of cigarette smoke exposure and/or nicotine treatment upon the development of gastric ulceration in mice. Histological changes (vasodilation, hemmorrhage, erosions, and infiltrations) in the gastric tissue will be evaluated. Experiments will be carried out to measure the biochemical (5-HT) as well as morphological changes in the gastrointestinal tract following (1) cessation of stress stimulation with continued tobacco smoke exposure or (2) in the absence of tobacco smoke exposure. The purpose of these experiments therefore, is to determine the extent to which tobacco smoke exposure or nicotine will contribute to a reversal of stress-induced gastric pathology after cessation of stress stimulation.

All of the proposed experiments will be carried out in mice, rats, or guinea pigs. All of the studies will be performed utilizing mice of either C3H strain, C57/BL6J strain, DBA-2 strain, and CF-1S strain. Male as well as female mice will be utilized to assess sex as well as strain differences. Rats (Sprague-Dawley and Long-Evans will be used in those studies concerned with cardiovascular tissue; where appropriate to consider strain differences, mice will be used in such studies. The studies on gastric tissue will be carried out in mice, rats and guinea pigs; the latter are particularly susceptible to stress-induced gastric ulceration and the tissues of various organs show an increase in 5-HT concentration upon acute exposure to cigarette smoke.

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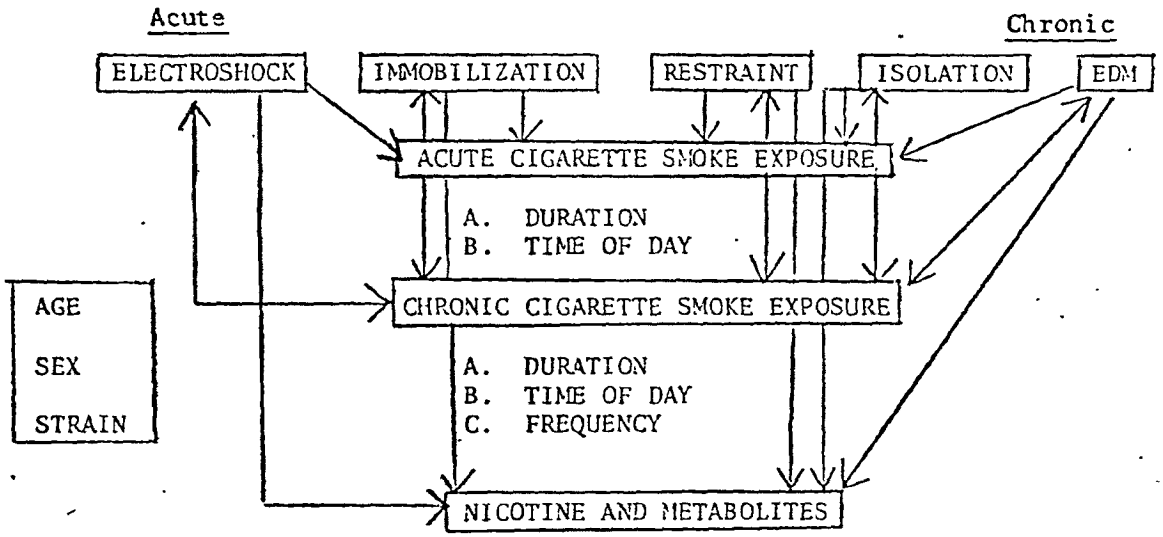
STRESS TOBACCO SMOKE INTERACTIONS:
INDEPENDENT VARIABLES AND SITES OF EFFECT



BRAIN

1. REGIONAL
   - CEREBRAL CORTEX
   - BASAL GANGLIA
   - DIENCEPHALON
   - LIMBIC REGION
   - CEREBELLUM
2. CELLULAR
   - NUERONS
   - GLIA
   - SYNAPTOSOMES
3. SUBCELLULAR
   - SYN. VESICLES
   - MEMBRANES
   - NUCLEI
   - MITOCHONDRIA
   - MICROSOMES

LUNG

1. EPITHELIAL TISSUE
2. PULM. ALVEOLAR MACROPHAGES
3. CELLULAR
   - SEPTAL CELLS
   - EPITHELIAL CELLS
   - KULSCHITSKY CELLS

HEART

1. REGIONAL
   - PERICARDIUM
   - MYOCARDIUM
2. CELLULAR
   - ENDOTHELIAL
   - PURKINUE
   - MYOC. FIBERS
3. SUBCELLULAR
   - NUCLEI
   - MITOCHONDRIA
   - MICROSOMES

G.I. TRACT

1. REGIONAL
   - FUNDUS
   - BODY
   - ANTRUM
   - PYLORIS
2. CELLULAR
   - MUCOSAL
   - SUBMUCOSAL
   - MUSCULARIS
   - ENTEROCHROMAFFIN
   - MAST

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10. Space and facilities available (when elsewhere than item 2 indicates, state location). Two large (approximately 800 square ft.) air-conditioned laboratories are completely equipped with all of the service facilities and permanent equipment necessary to carry out the proposed projects. Both laboratories are provided with ample space to accommodate the principal investigator and the laboratory technical staff. A separate office facility for the principal investigator and the grant project secretary is in use and this contains all of the necessary equipment (i.e., electric typewriter, APECO Copy Machine, etc.) to carry out the administrative portion of the grant research. Additional separate facilities include a vivarium in which separate rooms have been assigned specifically to the principal investigator for any special housing requirements necessary for rodents required as outlined in the grant proposal. Additionally, a histology laboratory with a full-time histologist, machine shop facility, with two full-time machinists, photograph laboratory with a full-time photographer, and electronics facility, with a full-time electronics technician, are all available to the principal investigator in connection with any specific requirements that the research protocol necessitates.

Basic equipment available in our existing research laboratories that will be specifically utilized in the conduct of the research proposed include a Beckman Ultra-Centrifuge, Sorvall High Speed Centrifuge, 3 Sorvall Table-top centrifuges, a Beckman DBG Spectrophotometer, Bausch & Lomb Spectrophotometer, Spectronic 20 Colorimeter, Farrand Spectrofluorometer, two Farrand Filter Fluorometers, 4 refrigerators, 3 freezers, a Kontes Glass Water Distillation Apparatus, and basic laboratory glassware and hardware. A Joelco Scanning Electron Microscope is available for use on a time-available basis.

11. Additional facilities required:

None

12 Biographical sketches of investigator(s) and other professional personnel (append)

Appended are biographical sketches of Dr. Walter B. Essman and Barbara Kornreich.

13. Publications (five most recent and pertinent of investigator(s); append list, and provide reprints if available).

See attached publication list.

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14. First year budget:

A. Salaries (give names or state "to be recruited") Professional (give % time of investigator(s) even if no salary requested)	% time	Amount
Walter B. Essman, M.D., Ph.D. Principal Investigator Sabbatical Leave Supplementation* from 9-1-76 to 12-31-76	100%	
Summer - 2/9ths	100%	REDACTED
Barbara Kornreich	100%	
Technical		
Nancy Mulligan (Secretary)	100%	REDACTED
Richard Rosenthal (Assistant Technician)	100%	
Plus 20% Fringe Benefits		
Sub-Total for A		

B. Consumable supplies (by major categories)

Chemicals	850.
Radiochemicals	1,500.
Centrifuge tubes, supplies	900.
Gases	400.
Glassware	780.
Animals	775.
Sub-Total for B	$5,205.

C. Other expenses (itemize) (Travel)

One domestic meeting and one international congress plus local travel	2,000.
Sub-Total for C	2,000.
Running Total of A + B + C	REDACTED

D. Permanent equipment (itemize)

NONE

Sub-Total for D	-----
E	$ 9,297.
Total request	$71,274.

*50% is requested for the first four months of the 76/77 Academic Year. 50% salary will be provided by the College for Sabbatical Leave. The Principal Investigator will devote 100% time to the research.

E. Indirect costs (15% of A+B+C)

15. Estimated future requirements:

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip.	Indirect Costs	Total
Year 2	REDACTED REDACTED	$5,205.00	$2,000.	------	$10,379.53	REDACTED
Year 3		$5,205.00	$2,000.	------	$ 8,700.42	

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16. Other sources of financial support:
List financial support from all sources, including own institution, for this and related research projects.

CURRENTLY ACTIVE

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates
"Metabolic Response to Stress - Tobacco Smoke Interactions"	RF-09267 C.T.R. #836A	$61,254.	1/1/75 to 12/31/75

PENDING OR PLANNED

Title of Project	Source (give grant numbers)	Amount	Inclusive Dates

It is understood that the investigator and institutional officers in applying for a grant have read and accept the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Principal investigator

Typed Name Walter B. Essman

Signature Walter B. Essman Date June 30, 1975

Telephone (212) 520-7619
Area Code Number Extension

Checks payable to

Research Foundation of C.U.N.Y.

Mailing address for checks

Mr. Paul Segall, Comptroller
Research Foundation of C.U.N.Y.
1411 Broadway
New York, New York 10018

Responsible officer of institution

Typed Name Hannah Petzenbaum, Res. Foundation Queens College.

Title

Signature David H. Spiedel Queens College Assoc. Dean of Faculty, Date 6/12/75

Telephone 6/12/75
Number Extension

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Biographical Sketch

Name: Walter B. Essman

Birthdate & Place: REDACTED

Citizenship: REDACTED

Social Security #: REDACTED

Education:
New York University, B.A.
University of North Dakota, M.A.
University of North Dakota, Ph.D.
University of Milan, M.D.

Post-Doctoral Training:
Senior Post-Doctoral Fellow (Neurophysiology)
Albert Einstein College of Medicine, Bronx, N. Y. 1959-1961.

Fellow, Dept. of Neurology (Neurochemistry)
Mt. Sinai Hospital, New York, N.Y. 1964-1968

Clinical Training: Rotating Internship and Residency in Internal Medicine

Licensure in Medicine:
New York State
State of Maine REDACTED

Military Service: U.S. Army, 1957-1957, Captain, MSC.

Academic Experience:
Professor (Psychology, Biochemistry), Queens College of the City University of New York, 1967 - Present.

Lecturer (Medicine), State University of N.Y. at Stony Brook, School of Medicine, 1974 - Present.

Associate Professor, Queens College of the City University of New York, 1965 - 1966.

Associate Professor, Queens College of the City University of New York, 1962 - 1964.

Research Professor, Neurology, Mt. Sinai School of Medicine New York, 1972 - 1974.

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Research Associate, Laboratory of Neurochemistry, Mt. Sinai School of Medicine, New York, 1966 - 1972

Research Assistant Professor, Department of Rehabilitation Medicine, Albert Einstein College of Medicine, 1962 - 1963.

Research Associate, Dept. of Physiology, Albert Einstein College of Medicine, 1961 - 1963.

Director, Psychophysiological Research, U.S. Army Surgical Research Unit, 1958 - 1959.

Membership in Professional Societies:

REDACTED

REDACTED

Other Professional Activities:

Associate Editor, Psychological Reports, 1959 - Present
Advisory Editor, Communications in Behavior
Consulting Editor, Physiology and Behavior, Journal of Neurobiology
Editor, Series in Modern Neurobiology, Spectrum Publications
Editor, Current Developments in Psycho . rmacology, Spectrum Publications, N.Y.

Honors and Awards:

Sigma Xi, 1957
Phi Delta Kappa, 1957
Ambrogino d'Oro - Municipality of Milan, 1971

Directory Listings:

Who's Who in Science
Who's Who in the East
American Men of Science
Outstanding Educators of America
Dictionary of International Biography

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R: REDACTED MATERIAL

Biographical Sketch

Name: Barbara Saplin Kornreich

Birthdate & Place: REDACTED

Citizenship: REDACTED

Social Security #: REDACTED

Education: State University of N.Y. at Albany, 1964, B.A.

Employment Experience:

New York Department of Health, Albany, N.Y., Assistant to post-doctoral fellow, Dr. M. Z. Atassi, 1963 - 1964

State University of New York at Buffalo, Sr. Research Assistant for Dr. M. Z. Atassi, Depts. of Biochemistry and Oral Biology, Schools of Medicine and Dentistry Duties: Protein research involving column chromatography, electrophoresis, Amino Acid analysis and immunochemical characterization techniques, 1964 - 1967.

Long Island Jewish Medical Center, New Hyde Park, N.Y. Sr. Research Associate to Dr. Morton Urivetzky. Duties: General supervision of laboratory operations; carried out research on collagen. All general procedures were used including the use of radio-immunoassay. 1967 - 1971.

Queens College of the City University of New York. Research Assistant to Dr. Walter B. Essman, Depts. of Psychology and Biochemistry: Research involves work with brain serotonin. 1973 - Present.

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